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**Title: Risk stratification of coronary heart disease in postmenopausal women using Framingham scale in Eastern Nepal.**

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**Risk stratification of coronary heart disease in postmenopausal women using Framingham scale in Eastern Nepal.**

**ABSTRACT**

**Introduction:**Cardiovascular disease (CVD) is one of the leading causes of mortality and morbidity in both developed and developing countries. CVD risk rises to double fold in women after menopause. We aim to stratify menopausal women of our region for having coronary heart disease in next 10 years.

**Methods:** One year cross sectional study from December 2012-December 2013 was conducted in General Out Patient Department (GOPD) of a tertiary care center of Eastern Nepal. The Standard ATP calculator was used and the relevant necessary data was introduced into the calculator and the automated result was collected.

**Results:** Among 272 participants above fifty percent had Framingham score 1-5%. And the risk was greater within first five years after menopause in 50-59 years of age group.Similarly, with advancing age and longer duration of menopause the risk became significantly higher.

**Conclusion:** Besides the established risk factors for CVD, postmenopausal state is additional risk for women and this study emphasizes this factor as risk of CVD even in our set up.

**Key words:**Cardiovascular Disease,Menopause, Framingham score, Postmenopausal women.

**INTRODUCTION**

Cardiovascular disease (CVD) has been the leading cause of mortality and morbidity of both men and women in developed as well as developing countries. CVD refer to disease affectingblood vessels and heart; and usually atherosclerosis associated.1Atherosclerotic plaques are thickened intima with various mixtures of fibrous tissues, cells, and lipid deposition with chronic inflammation.2, 3,4CVD risk factors are categorized into major independent risk factors and predisposing factors including several lifestyle variables and laboratory parameters.5The incidence and prevalence of coronary artery disease varies with the life cycle of women. The risk is lower in premenopausal state and increases in postmenopausal state. In comparison to 50-69 years females, there is significantly high morbidity and mortality due to CVD in women aged over 70 years accounting 54% of mortality and 39% total disability in developed nations.6This appears to be due to loss of ovarian function in post-menopausal women with deficiency of estrogen. The offspring’s of Framingham heart study who were gynecologically normal, and were not taking any hormones showed that menopause is positively correlated with LDL cholesterol and decreased LDL particle size.7CVD accounts for one third of all deaths and the rate is even higher for South Asian women.8

In country like Nepal, elderly women are under privileged, less literate, less health aware and health professionals are weakly concerned of advancing cardiovascular risk in this age group. American Heart Association (AHA) survey reveals that many (38%) women underestimate the importance of CVD risk and that this issue is not often discussed. This looses the opportunity to prevent CVD mortality and morbidity by lifestyle modifications.9Our study sets out to identify the risk score using Framingham risk assessment tool to predict the chance of having coronary heart disease in next 10 years. Here the subjects will get a chance to look at their future risk of developing coronary heart disease and the chance for timely intervention like life style modification and therapeutic intervention to prevent cardiovascular event.

**METHODS**

This was a yearlong observational study conducted in General Out Patient Department of tertiary care center of eastern Nepal.With permission from ethical clearance board and with informed consent, postmenopausal women attending GOPD and fulfilling the inclusion criteria were interviewed using a semi standardized Performa. This study was done from December 2012 to December 2013. Post-menopause for this study purpose was defined as cessation of menstruation naturally for at least one year. Inclusion criteria were menopause for at least one year and not having been diagnosed with a heart disease.Exclusion criteria were previously diagnosed heart disease, past history of stroke or transient ischemic attack, past history of hormonal treatment and past history of using lipid lowering agents. During a visit at General OPD, a medical history was taken, drug history, duration of menopause in years (DMY), cigarette smoking history were obtained. Smoker indicates any smoking in the past month.The blood pressure value used in the scoring is that obtained at the time of assessment, regardless of whether the patient is taking antihypertensive drugs. Blood pressure was assessed one time at the right upper arm after a 5 min rest in the sitting position with a manual mercury sphygmomanometer.Relevant anthropometric measurements, height, weight,and waist were measured with indoor clothes without shoes.

 Biomedical tests (Fasting Total Cholesterol (TC), High Density Lipoprotein-Cholesterol (HDL-C), and Fasting Blood Sugar (FBS) was done using a fasting venous blood sample after 12-hr fastat the central laboratory of the center on a voluntary fee pay basis and reports were collected on patient's follow up visits. Diabetes was defined as a fasting glucose level 140 mg/dL. The frequency, Mean and Standard deviation (SD) of demographic variables were measured. The relationship between DMY, TC, HDL-C were cross tabulated with Framingham score, where Framingham score was the dependent variable. Similarly, TC, HDL-C was also cross tabulated with DMY. Framingham score was calculated using the download version ATP Risk Estimator .xlsm 1.The ATP risk estimator in its current form does not include family history (FM) of heart disease, LDL-cholesterol and triglyceride level.The results was classified as risk of having a heart attack or dying from a heart disease within 10years. Low risk- Less than 10% chance, Intermediate risk- 10%-20% chance, High risk- more than 20% chance.Low risk (<10%) is further divided into Low 1- <1%, Low 2- 1-5%, Low 3- 6-<10%. All the data as recorded in the Performa was entered into the Excel database was analyzed by the SPSS-17 program (Chicago, IL, USA).

**RESULTS**

This study included 272 post-menopausal patients from July 2011 through June 2012 who presented with complaints other than cardiac. The age ranged from youngest 50years to oldest 80years. The duration of menopause ranged from 1-26years.The most common age to present in decades was in 6th decades (n=151) followed by 7th decades (n=83)(Table1)

**Table 1: Physical and clinical characteristics of subjects (n=272)**

|  |  |
| --- | --- |
| Characteristics | Mean(SD) |
| Age (in years) | 60.34(7.322) |
| Age of menopause (in years) | 7.24(6.313) |
| Systolic blood pressure (mmHg) | 127.92(15.680) |
| Total Cholesterol (mg/dl) | 178.55(44.165) |
| HDL (mg/dl) | 38.38(3.819) |
| Framingham 10 years risk estimation | 4.283 |

**Table 2. Variables of participants**

|  |  |  |
| --- | --- | --- |
| Variables  | Frequency | Percent |
| Age in decades | 50-59 | 151 | 55.5 |
| 60-69 | 83 | 30.5 |
| 70-79 | 35 | 12.9 |
| 80-89 | 3 | 1.1 |
| Duration of Menopause in Years (DMY) | 1-5 | 147 | 54.0 |
| 6-10 | 51 | 18.8 |
| 11-15 | 35 | 12.9 |
| 16-20 | 29 | 10.7 |
| 21-25 | 10 | 3.7 |
| Religion | Buddhist | 12 | 4.4 |
| Christian | 24 | 8.8 |
| Hindu | 212 | 77.9 |
| Kirat | 24 | 8.8 |
| Education | Illiterate  | 147 | 54 |
| Primary | 85 | 31.3 |
| Secondary | 24 | 8.8 |
| Higher | 16 | 5.9 |
| Occupation | Home maker | 118 | 43.4 |
| Farmer  | 74 | 27.7 |
| Business | 34 | 12.5 |
| Employed | 13 | 4.8 |
| Pension | 33 | 12.1 |
| Diet | Non-vegeterian | 249 | 91.5 |
| Vegeterian | 23 | 8.5 |
| Smoking  | Yes  | 194 | 71.3 |
| No  | 78 | 28.7 |
| Duration of exercise | Less than 150min/week | 12 | 4.4 |
| More than 150min/week | 5 | 1.8 |
| No exercise | 255 | 93.8 |
| Weight in Kgs | 40-49 | 28 | 10.3 |
| 50-59 | 151 | 55.5 |
| 60-69 | 63 | 23.2 |
| 70-79 | 26 | 9.6 |
| 80-89 | 4 | 1.5 |
| Waist in Cms | 60-69 | 23 | 8.5 |
| 70-79 | 154 | 56.6 |
| 80-89 | 72 | 26.5 |
| 90-99 | 18 | 6.6 |
| 100-109 | 5 | 1.8 |

This study showed 5.5% (n=15) had total cholesterol(TC) below 120mg/dl, 75.36% (n=205) had between 121-210mg/dl and 19.11% (n=52) had above 211mg/dl. Within first 5years of menopause 90 subjects had HDL-C <39 and the occurrence gradually decreased with the increase in DMY whereas those having HDL-C>50 didn’t gradually increase with increase in DMY (Table 3).

**Table 3: Relation between Duration of Menopause and total cholesterol and HDL-C**

|  |  |  |  |
| --- | --- | --- | --- |
| Lipid profile | Values in mg/dl | DMY (years) | p-value |
| **1 to 5** | **6 to 10** | **11 to 15** | **16 to 20** | **21 to 25** |
| Total cholesterol | <120 | 5 | 3 | 3 | 2 | 2 | 0.258 |
| 121-210 | 109 | 40 | 28 | 23 | 5 |
| >211 | 33 | 8 | 4 | 4 | 3 |
| Total | 147 | 51 | 35 | 29 | 10 |
| HDL | <39 | 90 | 24 | 22 | 21 | 6 | 0.260 |
|  40-49 | 56 | 27 | 13 | 7 | 4 |
| >50 | 1 | 0 | 0 | 1 | 0 |
| Total | 147 | 51 | 35 | 29 | 10 |

Similar pattern was recorded with age. Here 50% of the study population had SBP between 121-139mmHg and the result was not statistically significant with DMY and age.(Table 4)

Among total subjects, n=90, (30.73%) were diabetic and n=75 had low risk, n=14 had intermediate risk and n=1 had high risk score and the result was statistically significant.

**Chart 1: Distribution of 10 Yrs CHD Risk Score (Framingham Score)**

For Framingham score distribution, 89.7% of women had low risk (<10%), 9.9% had intermediate risk (10-20%) and 0.4% had high risk (>20%) of 10 yrs CHD risk. Similarly the occurrence of risk score was high in 50-59years of life followed by 60-69years and then 70-79years. A significant number (n=11)out of 27 of intermediate score were70-79years followed by n=7 were 50-69 years.(Chart 1)

With increase in duration of menopause, the Low risk (<10%) occurrence gradually decreased whereas the occurrence of High risk (>20%) didn’t increase in ascending order. From intermediate score group (N=27), n=9 had the longest duration of menopause (20-25years) (Table 4)

**Table 4: Relation between DMY, Total cholesterol, HDL-C &Framingham score**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variables | Low (<10%) | Intermediate (10-20%) | High (>20%) | p-value |
| DMY(Years) | 1-5 | 140 | 7 | 0 | **˂0.001** |
| 6-10 | 47 | 4 | 0 |
| 11-15 | 31 | 3 | 1 |
| 16-20 | 25 | 4 | 0 |
| 21-25 | 1 | 9 | 0 |
| **Total** | **244** | **27** | **1** |
| Total Cholesterol (mg/dl) | <120 | 14 | 1 | 0 | **˂0.001** |
| 121-210 | 194 | 11 | 0 |
| >211 | 36 | 15 | 1 |
| **Total** | **244** | **27** | **1** |
| HDL-C(mg/dl) | <39 | 44 | 18 | 1 | 0.741 |
| 40-49 | 98 | 9 | 0 |
| >50 | 2 | 0 | 0 |
| **Total** | **244** | **27** | **1** |

The cross tabulation of TC and Framingham score showed statically significant result with n=205 having TC 121-210mg/dL and n=52 having >211mg/dL and one subject from this group had high risk score.(Table 6) The cross tabulation between HDL-C and Framingham score was not statically significant. Among t=272, n=163 had HDL-C <39 and n=1(t=163) had high risk score.(Table 4)

**DISCUSSION**

Several studies on increasing cardiovascular risk in post-menopausal women put insight in importance of early screening and timely intervention for primary prevention. Here in this studyFramingham Risk assessment tool has been used to calculate the 10years CHD risk and traditional CVD risk factors have been assessed.Among 272subjects,more than three quarters n= 244 subjects (89.7%), had projected 10 years risk of CHD risk <10%. The outcome was quite different in a comparative study with total 691 subjects aged 30-70 years , n=59 subjects (8.5%) had projected 10 year coronary heart disease risks > 30%, and 291 (42.1%) had risks > 15%.10

The mean Framingham risk estimation of participants in this study was 4.28 which are comparable with a study done on Iranian postmenopausal women with mean risk 1.46. The estimated 10 years risk for CHD was greater in this study, which could be because the mean age of the participants was high (mean age =60.34years) and it hasadopted the calculator from the original Framingham study but the performance of the scale in Asian population is not clear.11This study illustrates 20% of study population had TC >211mg/dL and the occurrence(n=146) of TC>121mg/dLwas in age group 50-59 years. The highest number of subjects (n=142) developed this after 1-5years of menopause and this was 54% rise in CHD risk and was found to decline gradually in the following ages. A study by Mathews et al. in SWAN (Study of Women's Health across the Nation), discussed that total cholesterol, LDL-C, HDL-C changes with menopause in first 1 year. And several studies also have shown a strong positive relationship of total cholesterol (TC) above 180mg/dl with CHD risk and death.12,13

On the basis of those studies, the rise in CHD risk in first few years of menopause is implacable to the postmenopausal women of this study group. And this issue is addressed by ATPIII of the National Cholesterol Education Program (NCEP) guideline which suggests that if one's FRE is <10% with 2+ risk factors, one's LDL goal should be <130, and individuals with FRE <10% with 0 to 1 risk factors should have a LDL goal of <160.

Similarly, several other studies have established a powerful protective inverse relation between increasing HDL and incidence of CHD. Low HDL concentrations less than 40mg/dl have a greater risk for CHD.14In this study, 59.92% (n=163) (total n=272) of participants had HDL less than 39, among this (n=92) had 10years CHD risk between 1-5%. Who had menopause within last 1-5 years (n=90) had HDL <39mg/dL. This result is comparable with the result from a study done on Iranian postmenopausal women which showed only 22.4% of participants with HDL less than 40. This indicates that the women from our region are at higher risk for CHD than Iranian women.

The recent studies on post-menopausal women and CVD risk also states the risk steepen after post-menopause state due to loss of protective effects of estrogen and risk is significantly higher with long duration of menopause similar to our findings.15,16

**CONCLUSION**

The Framingham risk was comparatively greater within first five years after menopause in 50-59years of age group. With advancing age and longer duration of menopause the Framingham risk became gradually higher. So, postmenopausal state is an additional risk for CVD in women even in our set up.

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